

BIOGRAPHICAL SKETCH

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NAME: Alberto Danielli

CONTACT: alberto.danielli@unibo.it

Institutional Home Page: <https://www.unibo.it/sitoweb/alberto.danielli/en>

Molecular Biotechnology Lab: <https://site.unibo.it/molecular-biotechnology-lab/en>

ORCID 0000-0002-9414-9898

University of Bologna

FaBiT – Department of Pharmacy and Biotechnology, Via Selmi, 3 – 40126 Bologna (Italy)

POSITION TITLE: Associate Professor of Molecular Biology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Bologna, Italy	MSc	03/1996	Agricultural Sciences; Plant Pathology, Molecular Insect Biology
EMBL Heidelberg – University of Heidelberg, Germany	PhD	10/2001	Molecular Biology; Molecular cell biology of insect immune responses; malaria parasite transmission
University of Bologna, Italy	Post-doc	07/2005	Molecular Microbiology; Transcriptional Regulation

A. Personal Statement

I am a driven molecular biologist, with a strong background in molecular microbiology, molecular cell biology of infectious pathogens and disease as well as biotherapeutic vectors. My current research focuses on fundamental aspects of microbial gene regulation and phage bionanotechnologies. As PI or co-Investigator of several national and European-funded research grants, I contributed to the understanding of the transcriptional responses of the obliged human pathogen *Helicobacter pylori*. In particular, I laid the groundwork for using chromatin-immunoprecipitation to dissect the transcriptional regulatory network of this bacterium and systematically characterized the metal-dependent responses governed by the central Fur and NikR regulators. This work produced several important and well-cited contributions published in top journals (1,2). Since 2016 I further head the Molecular Biotechnology Laboratory (MBTlab) in which the development of innovative biotherapies and biosensors based on the molecular engineering of bacteriophages and of self-assembling protein nanoparticles is pursued (3, 4). This research led to the presentation and granting of several patent applications (5) and to the foundation of a SpinOFF company. As a result of present and past activities and research achievements, I was recently affiliated to the Preclinical Research in Oncology Unit of the University Hospital of Bologna IRCCS, Sant' Orsola Polyclinic, an integrated organization in the national, regional and local system for health and scientific research, as well as to the CIB Consorzio Interuniversitario per le Biotechnologie, a well-established partnership of Italian universities for the promotion of biotechnological research.

Granting ID; highlight of main ongoing and completed projects:

Oct2023 – present	PRIN2022 (2022A5YWJJ) - Principal Investigator – Photoglioblaster: Innovative photo-sonodynamic therapy approaches for targeted treatment of brain tumors: application to glioblastoma
May2022 – present	EIC Pathfinder Open – WP Task Leader – ECLipse: ECL-based Infectious Pathogen (bio)Sensor
Sep2022 – present	PRIN2020 (2020WMSNBL) - Principal Investigator - Wireless and non-genetic photostimulation of neurons by cell-specific targeting of photovoltaic nanoparticles: application to neurodegenerative diseases of retina and brain
Sep2021 - Feb2022	FISR2020 – Principal Investigator - ph2ph: Phage-based biosensor for the direct detection of Sars-CoV-2
Feb2021 - May2022	Proof-of-Concept competitive Grant (Ministry of Economic Development -MISE) – Principal Investigator - Modular phage vector platform for sonodynamic therapy
Jun2021– present	JPND (EU Joint Programme - Neurodegenerative Disease) Grant – WP leader – NeuroPhage: Phage-based targeted neural stimulation in neurodegenerative diseases
Jan2020 – present	AIRC MFAG Grant (Italian Cancer Research Association) – Team Member - NanoPhage: An Innovative Hybrid Platform for Targeted Sono- Photo- Dynamic Cancer Therapy
2010 - 2011	PRIN grant (MIUR) – Team Member - Unraveling structural and functional determinants behind Helicobacter pylori pathogenesis and persistence
2008	Fondazione Del Monte competitive Grant - Principal Investigator - Regulation of cag virulence genes in the gastric pathogen Helicobacter pylori
2007	PRIN (Italian University ad Research Ministry MIUR) - Principal Investigator - Molecular characterization of Helicobacter pylori virulence factors

Selected Publications:

1. Roncarati D, Pelliciani S, Doniselli N, Maggi S, Vannini A, Valzania L, Mazzei L, Zambelli B, Rivetti C*, **Danielli A***. Metal-responsive promoter DNA compaction by the ferric uptake regulator. Nat Commun. 2016 Aug 25;7:12593. (*corresponding)
2. Agriesti F, Roncarati D, Musiani F, Del Campo C, Iurlaro M, Sparla F, Ciurli S, **Danielli A***, Scarlato V. FeON-FeOFF: the Helicobacter pylori Fur regulator commutates iron-responsive transcription by discriminative readout of opposed DNA grooves. Nucleic Acids Res. 2014 Mar;42(5):3138-51. (*corresponding)
3. M, Flammini S, Montrone M, Sanità G, De Felice V, Mattioli EJ, Zangoli M, Ulfo L, Nigro M, Rossi T, Di Giosia M, Esposito E, Di Maria F, Tino A, Tortiglione C*, **Danielli A***, Calvaresi M*. Phage-Templated Synthesis of Targeted Photoactive 1D-Thiophene Nanoparticles. Small. 2024 Nov 5:e2405832. (*corresponding)
4. Turrini E, Ulfo L, Costantini PE, Saporetto R, Di Giosia M, Nigro M, Petrosino A, Pappagallo L, Kaltenbrunner A, Cantelli A, Pellicioni V, Catanzaro E, Fimognari C, Calvaresi M*, **Danielli A***. Molecular engineering of a spheroid-penetrating phage nanovector for photodynamic treatment of colon cancer cells. Cell Mol Life Sci. 2024 Mar 17;81(1):144. (*corresponding)
5. Modular phage vector platform for sonodynamic therapy WO2020261199

B. Positions, Scientific Appointments, and Honors

2024	ANR France, PEPR-BBIT Priority Research Programme Biotherapy and Bioproduction of Innovative Therapies; Panel Member of Scientific Evaluation Committee;
2024 – present	Department Board, Department of Pharmacy and Biotechnology, University of Bologna
2024 – present	Research Affiliate IRCCS Azienda Ospedaliero Universitaria Sant'Orsola, Bologna
2024 – present	Member, SIBBM Italian Society of Biophysics and Molecular Biology
2023 – present	CIB Consorzio Interuniversitario per le Biotecnologie, University delegate;
2023 – present	Associate Editor, Frontiers in Microbiology;
2023 – present	Bionys spinoff company, founding partner
2022 – present	PQA Quality Assurance Board, University of Bologna, member

2022 – present	Member, SIFB Italian Society of Photobiology
2021	ANR France, CE11 Scientific Committee, panel member
2018 – present	PhD programme in Cellular and Molecular Biology; Faculty member
2015 – present	Associate Professor, Dept. Pharmacy and Biotechnology, University of Bologna, ITA
2014-2022	Institute Pasteur (F), ad hoc reviewer for PTR Research Proposals
2009	Atomium Culture, featured scientist. Selected by the EU-funded Permanent Platform for European Excellence for the dissemination of leading European research.
2007 – present	Member, SIMGBM Italian Society of General Microbiology and Microbial Biotechnologies
2005-2015	Assistant Professor, Department of Biology, University of Bologna, ITA

C. Contributions to Science

1. In the Kafatos group at EMBL Heidelberg, and in collaboration with the laboratory of Insect Immunity led by J.A Hoffman at CNRS-IMBB Strasbourg, my early publications addressed the characterization of immunity-related genes and gene families in the malaria vector *Anopheles gambiae*. In particular, these studies led to the identification of a modular chitin-binding protease associated with hemocytes and hemolymph in the mosquito, as well to the cloning and characterization of four alternatively spliced serpin isoforms, differentially induced in the midgut by malaria ookinete invasion. I demonstrated that in response to midgut epithelial invasion, one isoform translocates from the nucleus to the cytoplasm and is strongly overexpressed, while the invaded cells exhibit signs of apoptosis, suggesting a link between this type of intracellular serpin and epithelial damage. These publications provided for the first time a comprehensive insight in the molecular and cellular mechanisms taking place during ookinete midgut invasion, underlying vector competence and development of effective malaria ookinete transmission blocking strategies.
 - a. **Danielli A**, Loukeris TG, Lagueux M, Müller HM, Richman A, Kafatos FC. A modular chitin-binding protease associated with hemocytes and hemolymph in the mosquito *Anopheles gambiae*. *Proc Natl Acad Sci U S A*. 2000 Jun 20;97(13):7136-41..
 - b. Christophides GK, Zdobnov E, Barillas-Mury C, Birney E, Blandin S, Blass C, Brey PT, Collins FH, **Danielli A**, Dimopoulos G, Hetru C, Hoa NT, Hoffmann JA, Kanzok SM, Letunic I, Levashina EA, Loukeris TG, Lycett G, Meister S, Michel K, Moita LF, Müller HM, Osta MA, Paskewitz SM, Reichhart JM, Rzhetsky A, Troxler L, Vernick KD, Vlachou D, Volz J, von Mering C, Xu J, Zheng L, Bork P, Kafatos FC. Immunity-related genes and gene families in *Anopheles gambiae*. *Science*. 2002 Oct 4;298(5591):159-65.
 - c. **Danielli A**, Kafatos FC, Loukeris TG. Cloning and characterization of four *Anopheles gambiae* serpin isoforms, differentially induced in the midgut by *Plasmodium berghei* invasion. *J Biol Chem*. 2003 Feb 7;278(6):4184-93.
 - d. **Danielli A**, Barillas-Mury C, Kumar S, Kafatos FC, Loukeris TG. Overexpression and altered nucleocytoplasmic distribution of *Anopheles* ovalbumin-like SRPN10 serpins in *Plasmodium*-infected midgut cells. *Cell Microbiol*. 2005 Feb;7(2):181-90.
2. Eventually I joined the group of Molecular Microbiology led Prof. V.Scarlato at the University of Bologna, first as a post-doc and then as tenured Research Assistant Professor. In these roles I followed several specific research projects and secured external funding to support my work as independent PI. These studies focused on the systematic genome-wide dissection of the *H. pylori* transcriptional regulatory circuits. I directly characterized the molecular mechanisms and allosteric behaviour of two fundamental metal-dependent regulators, Fur and NikR, including discriminative readout of minor and major DNA grooves, DNA looping at promoters and complex regulatory interactions between the regulators. This body of work involved both molecular and genomic approaches allowing to dissect the protein-DNA interactions in great detail, both in vitro and in vivo. The research permitted to better comprehend the systems biology behind the persistence of *H. pylori* in the human gastric niche, the transcriptional regulation of the *cag* pathogenicity island genes, and also highlighted the contribution of small RNAs in the pathobiology of the bacterium. These studies set myself as recognized and independent scientist in the national and international molecular microbiology community, as also acknowledged by promotion to Associated Professor of Molecular Biology at the University of Bologna in 2015. (see also selected citations in Personal Statement)

- a. **Danielli A**, Scarlato V. Regulatory circuits in *Helicobacter pylori* : network motifs and regulators involved in metal-dependent responses. *FEMS Microbiol Rev.* 2010 Sep;34(5):738-52.
 - b. Vannini A, Roncarati D, **Danielli A**. The cag-pathogenicity island encoded CncR1 sRNA oppositely modulates *Helicobacter pylori* motility and adhesion to host cells. *Cell Mol Life Sci.* 2016 Aug;73(16):3151-68.
 - c. Vannini A, Pinatel E, Costantini PE, Pellicciari S, Roncarati D, Puccio S, De Bellis G, Peano C, **Danielli A**. Comprehensive mapping of the *Helicobacter pylori* NikR regulon provides new insights in bacterial nickel responses. *Sci Rep.* 2017 Apr 10;7:45458.
 - d. Vannini A, Pinatel E, Costantini PE, Pellicciari S, Roncarati D, Puccio S, De Bellis G, Scarlato V, Peano C, **Danielli A**. (Re)-definition of the holo- and apo-Fur direct regulons of *Helicobacter pylori*. *J Mol Biol.* 2024 May 15;436(10):168573.
3. Leveraging on the broad interdisciplinary expertise gained in these years, I recently became interested also in bionanotechnological applications of bacteriophages and self-assembling protein nanoparticles as targetable biotherapeutics and biosensors. My lab pioneers the engineering of harmless M13 phages as a multifunctional vector platform, enabling the selective photo/sono-ablation of ESKAPEE priority pathogens and tumors. We have developed a technology able to take advantage of the well-defined molecular biology of M13 to functionalize its capsid with hundreds of photo- or sono-activable sensitizers and contemporarily target this triggerable nanobot to specific cancer markers and bacterial species by phage display of peptide targeting moieties, including single domain/chain antibodies. Upon functionalization with fluorophores or luminophores, the same platform can also be used as signal-amplifying transduction element for highly sensitive diagnostic applications. These findings contribute to the development of modular next-generation biosensors and nanobiotherapeutics. In the framework of these studies I have supported and supervised 5 post-doctoral fellows and 5 PhD students and a tenured Research Assistant. (see also selected publications in Personal Statement)
- a. Cantelli A, Piro F, Pecchini P, Di Giosia M, **Danielli A***, Calvaresi M*. Concanavalin A-Rose Bengal bioconjugate for targeted Gram-negative antimicrobial photodynamic therapy. *J Photochem Photobiol B.* 2020 Mar 13;206:111852. (*corresponding)
 - b. Ulfo L, Cantelli A, Petrosino A, Costantini PE, Nigro M, Starinieri F, Turrini E, Zadran SK, Zuccheri G, Saporetti R, Di Giosia M, **Danielli A***, Calvaresi M*. Orthogonal nanoarchitectonics of M13 phage for receptor targeted anticancer photodynamic therapy. *Nanoscale.* 2022 Jan 20;14(3):632-641. (*corresponding)
 - c. Ulfo L, Costantini PE, Di Giosia M, **Danielli A***, Calvaresi M*. EGFR-Targeted Photodynamic Therapy. *Pharmaceutics.* 2022 Jan 20;14(2):241. (*corresponding)
 - d. Petrosino A, Saporetti R, Starinieri F, Sarti E, Ulfo L, Boselli L, Cantelli A, Morini A, Zadran SK, Zuccheri G, Pasquini Z, Di Giosia M, Prodi L, Pompa PP, Costantini PE*, Calvaresi M*, **Danielli A***. A modular phage vector platform for targeted photodynamic therapy of Gram-negative bacterial pathogens. *iScience.* 2023 Sep 27;26(10):108032. (*corresponding)
 - e. Ahmed H, Lopez H, Boselli F, Tarricone G, Vercellino S, Costantini PE, Castagnola V, Veronesi M, Benfenati F, **Danielli A**, Boselli L, Pompa PP. Biomimetic Plasmonic Nanophages by Head/Tail Self-Assembling: Gold Nanoparticle/Virus Interactions. *ACS Nano.* 2024 Aug 13;18(32):21302-21315.

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